

pending case

APPENDIX

Pending Claims Prior to Restriction Requirement

U.S. Patent Application No. 09/578,453

PHARMACEUTICAL COMPOSITIONS AND UTILIZATION THEREOF PARTICULARLY FOR THE
TREATMENT OF NEURODEGENERATIVE DISORDERS

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16. A recombinant virus selected from the group consisting of adenovirus, adeno-associated virus and herpes virus, said recombinant virus comprising a nucleic acid selected from the group consisting of:
 - (a) nucleic acids encoding a mutated form of p53 which antagonizes wild-type p53-mediated neuronal cell degeneration *in vitro*;
 - (b) the site for binding of p53 to DNA; and
 - (c) nucleic acids encoding an antisense RNA which inhibits expression of p53.
17. A recombinant virus according to claim 16, wherein said virus is an adenovirus.
18. A recombinant virus according to claim 16, wherein the nucleic acid comprises SEQ ID No. 2 or an active variant thereof.
19. A recombinant virus according to claim 16, wherein said virus comprises two nucleic acids selected from the group consisting of:
 - (a) nucleic acids encoding a mutated form of p53 which antagonizes wild-type p53-mediated neuronal cell degeneration;
 - (b) the site for binding of p53 to DNA; and
 - (c) nucleic acids encoding an antisense RNA which inhibits expression of p53.

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20. A recombinant virus according to claim 16, wherein said virus is a replication defective virus.
21. A recombinant virus according to claim 16, wherein the nucleic acid encodes the p53Val135 mutated form of p53.
22. A method of inhibiting toxicity in cultured neuronal cells comprising administering to said cells a nucleic acid selected from the group consisting of:
 - (a) nucleic acids encoding a mutated form of p53 which antagonizes wild-type p53-mediated neuronal cell degeneration *in vitro*;
 - (b) the site for binding of p53 to DNA; and
 - (c) nucleic acids encoding an antisense RNA which inhibits expression of p53.
23. The method according to claim 22, wherein the nucleic acid is a p53 antisense oligonucleotide.
24. The method of claim 23, wherein said oligonucleotide has the sequence of SEQ ID No. 1.
25. The method according to claim 22, wherein the nucleic acid is within a vector.
26. The method according to claim 25, wherein the vector is a replication defective virus.
27. A method for identifying compounds which at least partially inhibit the activity of the p53 protein, comprising the steps of:

- (a) treating a culture of neuronal cells sensitive to glutamate-induced excitotoxicity with a compound so that said compound enters said neuronal cells;
- (b) adding an excitotoxic amount of glutamate to the culture medium of said neuronal cells.
- (c) comparing the amount of excitotoxicity measured in said neuronal cells with the amount of excitotoxicity measured in neuronal cells which were not treated with said compound.

- 28. The method according to claim 27, wherein the neuronal cells are embryonic rat cortical neurons.
- 29. The method according to claim 27, wherein the compound is a recombinant virus according to claim 16.
- 30. The method according to claim 27, wherein the compound is a p53 antisense oligonucleotide.
- 31. The method according to claim 27, wherein the compound is a recombinant virus according to claim 19.